

CLAIMS

1. An isolated polypeptide that specifically binds to a neoplastic cell or a cell of a pre-cancerous lesion, but does not specifically bind to a normal cell, wherein said isolated
5 polypeptide comprises amino acids 11-15, 30-46, and 79-88 of SEQ ID NO:2, and wherein said normal cell is not a cell of the glomerular, fascicular zone of the adrenal gland or an epithelial cell of the collection tubes of the kidney.

2. The isolated polypeptide of claim 1, wherein said polypeptide comprises the
10 sequence of SEQ ID NO:2.

3. The isolated polypeptide of claim 1, wherein said polypeptide further comprises amino acids 17-32, 48-54, and 87-95 of SEQ ID NO:4.

4. The isolated polypeptide of claim 3, wherein said polypeptide comprises the
15 sequence of SEQ ID NO:4.

5. The isolated polypeptide of claim 1, wherein said polypeptide is capable of inducing apoptosis of said neoplastic cell or said cell of said pre-cancerous lesion, but does
20 not induce apoptosis of said normal cell.

6. The isolated polypeptide of claim 1, wherein said neoplastic cell is selected from the group consisting of Barrett's tumors and tumors of the esophagus, stomach, intestine, rectum, liver, gallbladder, pancreas, lungs, bronchi, breast, cervix, prostate, heart, ovary, and
25 uterus.

7. The isolated polypeptide of claim 1, wherein said pre-cancerous lesion is selected from the group consisting of dysplasia of the gastric mucosa, interstitial metaplasia of the stomach, inflammation of the gastric mucosa which is associated with the bacteria
30 *Helicobacter pylori*, tubular and tubulovillous adenomas of the stomach, tubular adenoma of

the colon, villous adenoma of the colon, dysplasia in ulcerative colitis, Barrett's dysplasia, Barrett's metaplasia of the esophagus, cervical intraepithelial neoplasia I, cervical intraepithelial neoplasia II, cervical intraepithelial neoplasia III, squamous epithelial metaplasia, squamous epithelial dysplasia of the bronchus, low grade and high grade prostate intraepithelial neoplasia (PIN), breast ductal carcinoma in situ (D-CIS), and breast lobular carcinoma in situ (L-CIS).

8. The isolated polypeptide of claim 1, wherein said polypeptide is a functional fragment of an antibody selected from the group consisting of V_L, V_H, F_V, F_C, Fab, Fab', and F(ab')₂.

9. The isolated polypeptide of claim 1, wherein said polypeptide specifically binds to a polypeptide comprising SEQ ID NO:6.

10. An isolated nucleic acid molecule comprising nucleic acids 31-45, 88-138, and 235-264 of SEQ ID NO:1.

11. The isolated nucleic acid molecule of claim 10, wherein said nucleic acid molecule comprises the sequence of SEQ ID NO:1.

12. An isolated nucleic acid molecule comprising nucleic acids 49-96, 142-162, and 259-285 of SEQ ID NO:3.

13. The isolated nucleic acid molecule of claim 12, wherein said nucleic acid molecule comprises the sequence of SEQ ID NO:3.

14. An isolated nucleic acid molecule comprising the sequence of SEQ ID NO:5.

15. A vector comprising the nucleic acid sequence of SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

16. An isolated cell comprising the vector of claim 15.

17. An isolated cell that expresses the polypeptide of claim 1.

18. The isolated cell of claim 17, wherein said isolated cell is a mammalian cell.

19. The isolated cell of claim 18, wherein said mammalian cell is a human cell.

20. A method of producing the purified polypeptide of claim 1, said method comprising contacting a cell with a vector comprising SEQ ID NO:1 and isolating the polypeptide expressed by said vector.

21. The method of claim 20, wherein said vector further comprises the sequence of SEQ ID NO:3.

22. A method of diagnosing a neoplasm or a pre-cancerous lesion in a mammal, said method comprising the steps of, (a) contacting a cell or tissue sample derived from said mammal with the purified polypeptide of claim 1, and (b) detecting whether said purified polypeptide specifically binds to said cell or tissue sample, wherein specific binding of said purified polypeptide to said cell or tissue sample is indicative of said mammal having a neoplasm or pre-cancerous lesion.

23. The method of claim 22, wherein said cell or tissue sample is derived from a tissue selected from the group consisting of Barrett's tumors, tumors of the esophagus, stomach, intestine, rectum, liver, gallbladder, pancreas, lungs, bronchi, breast, cervix, prostate, heart, ovary, and uterus, dysplasia of the gastric mucosa, interstitial metaplasia of the stomach, inflammation of the gastric mucosa which is associated with the bacteria *Helicobacter pylori*, tubular and tubulovillous adenomas of the stomach, tubular adenoma of the colon, villous adenoma of the colon, dysplasia in ulcerative colitis, Barrett's dysplasia,

Barrett's metaplasia of the esophagus, cervical intraepithelial neoplasia I, cervical intraepithelial neoplasia II, cervical intraepithelial neoplasia III, squamous epithelial metaplasia, squamous epithelial dysplasia of the bronchus, low grade and high grade prostate intraepithelial neoplasia (PIN), breast ductal carcinoma in situ (D-CIS), and breast lobular carcinoma in situ (L-CIS).

24. The method of claim 22, wherein said mammal is a human.

25. The method of claim 22, wherein said polypeptide is an antibody.

26. The method of claim 25, wherein said polypeptide is murine antibody 58/47-69.

27. The method of claim 22, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

28. The method of claim 27, wherein said detectable agent is capable of inducing apoptosis of said cell.

29. The method of claim 22, wherein said polypeptide is conjugated to a protein purification tag.

30. The method of claim 29, wherein said protein purification tag is cleavable.

31. A method of treating a proliferative disorder in a mammal, said method comprising the step of contacting a cell with the purified polypeptide of claim 1, wherein binding of said purified polypeptide to said cell results in the induction of apoptosis of said cell.

32. The method of claim 31, wherein said mammal is a human.

33. The method of claim 31, wherein said polypeptide is an antibody.

34. The method of claim 33, wherein said polypeptide is a humanized antibody.

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35. The method of claim 33, wherein said antibody is murine antibody 58/47-69.

36. The method of claim 31, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

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37. The method of claim 31, wherein said polypeptide is conjugated to a protein purification tag.

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38. The method of claim 37, wherein said protein purification tag is cleavable.

39. A pharmaceutical composition comprising the isolated polypeptide of claim 1 in a pharmaceutically acceptable carrier.

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40. A diagnostic agent comprising the isolated polypeptide of claim 1.

41. An isolated polypeptide, wherein said polypeptide comprises an amino acid sequence consisting of amino acids 469-518 of SEQ ID NO:6 or amino acids 739-748 of SEQ ID NO:6, and wherein said polypeptide does not comprise the full-length sequence of SEQ ID NO:6.

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42. The isolated polypeptide of claim 41, wherein said polypeptide comprises an amino acid sequence consisting of amino acids 469-518 of SEQ ID NO:6.

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43. The isolated polypeptide of claim 41, wherein said polypeptide comprises an

amino acid sequence consisting of amino acids 739-748 of SEQ ID NO:6.

44. The isolated polypeptide of claim 41, wherein said polypeptide is at least 95% pure.

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45. The isolated polypeptide of claim 41, wherein said polypeptide is specifically bound by murine antibody 58/47-69.

46. The isolated polypeptide of claim 41, wherein said polypeptide comprises a tumor-specific glycostructure.

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47. The isolated polypeptide of claim 41, wherein said polypeptide is expressed by a pre-cancerous lesion selected from the group consisting of dysplasia of the gastric mucosa, interstitial metaplasia of the stomach, inflammation of the gastric mucosa which is associated with the bacteria *Helicobacter pylori*, tubular and tubulovillous adenomas of the stomach, tubular adenoma of the colon, villous adenoma of the colon, dysplasia in ulcerative colitis, Barrett's dysplasia, Barrett's metaplasia of the esophagus, cervical intraepithelial neoplasia I, cervical intraepithelial neoplasia II, cervical intraepithelial neoplasia III, squamous epithelial metaplasia, squamous epithelial dysplasia of the bronchus, low grade and high grade prostate intraepithelial neoplasia (PIN), breast ductal carcinoma in situ (D-CIS), and breast lobular carcinoma in situ (L-CIS), and not by normal cells of the same tissue type.

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48. The isolated polypeptide of claim 41, wherein said polypeptide is expressed by a tumor selected from the group consisting of Barrett's tumors and tumors of the esophagus, stomach, intestine, rectum, liver, gallbladder, pancreas, lungs, bronchi, breast, cervix, prostate, heart, ovary, and uterus, and not by a normal cell of the same tissue type.

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49. A pharmaceutical composition comprising the polypeptide claim 41 in a pharmaceutically acceptable carrier.

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50. A diagnostic agent comprising the isolated polypeptide of claim 41.

51. A method of inducing a tumor-specific immune response in a mammal, said method comprising the step of contacting said mammal with an isolated polypeptide comprising the sequence of SEQ ID NO:6, or a fragment comprising amino acids 469-518 of SEQ ID NO:6 or amino acids 739-748 of SEQ ID NO:6, wherein said contacting induces a tumor-specific immune response in said mammal.

52. The method of claim 51, wherein said tumor-specific immune response comprises the production of an antibody that induces apoptosis of a cell which is specifically bound by said antibody.

53. The method of claim 51, wherein said fragment comprises amino acids 469-518 of SEQ ID NO:6 and amino acids 739-748 of SEQ ID NO:6 and does not comprise the full-length sequence of SEQ ID NO:6.

54. A method of producing an isolated polypeptide comprising the sequence of SEQ ID NO:6 or a fragment thereof comprising amino acids 469-518 of SEQ ID NO:6 or amino acids 739-748 of SEQ ID NO:6, said method comprising the steps of (a) contacting a cell with a vector comprising a nucleic acid sequence that is substantially identical to SEQ ID NO:5 and (b) isolating the polypeptide expressed by said cell.

55. A method of identifying a candidate therapeutic compound, said method comprising the steps of (a) contacting a cell expressing a polypeptide comprising the amino acid sequence of SEQ ID NO:6, or a fragment thereof comprising amino acids 469-518 of SEQ ID NO:6 or amino acids 739-748 of SEQ ID NO:6, with a test compound and (b) determining whether said test compound induces apoptosis of said cell and not of a control cell contacted with said test compound, wherein a test compound that induces apoptosis of said cell and not of said control cell is a candidate therapeutic compound.

56. The method of claim 55, wherein said fragment comprises amino acids 469-518 of SEQ ID NO:6 and amino acids 739-748 of SEQ ID NO:6 and does not comprise the full-length sequence of SEQ ID NO:6.

- 5 57. The method of claim 55, wherein said cell is adenocarcinoma cell line 23132 (DSMZ Accession No. DSM ACC 201).